Amendments To The Drawings

A Replacement Sheet for Figure 1 is attached, in which the duplicative label on the "y" axis has been deleted.

Remarks/Arguments

Claims 1-17 and 35-38 are pending. Claims 18-34 have been withdrawn due to restriction. Claim 17 has been amended herein.

The Examiner has objected to the drawings because Figure 1 contains a duplicate label on the y axis. Applicants have provided herein a replacement sheet for figure 1 in which the duplicate label has been removed. Therefore, Applicants respectfully request the withdrawal of this objection.

Claim 17 has been objected to due to a typographical error. Applicants thank the Examiner for pointing out the error. Applicants have corrected the error by amendment above and respectfully request the withdrawal of this objection.

Claim 15 has been rejected under 35 U.S.C. § 102(e) as being anticipated by USPN 6,617,333 (Rabindran, et al.), which discloses an antineoplastic combination of CCI-779 and EKB-569. Applicants traverse this rejection for the reasons set forth below.

Claim 15 is drawn to a stabilized pharmaceutical composition containing at least one basic excipient in a concentration sufficient to bring the pH of the composition to at least 8, and at least one pharmaceutically acceptable excipient. The cited patent does not teach such a stabilized composition.

The Examiner has noted that the cited patent lists excipients that include basic excipients. However, the patent does not disclose that one needs to select such an excipient and that one needs to use enough of such an excipient to achieve a pH of at least 8 in order to achieve a stabilized composition according to the present invention. In fact, in the same sentence where calcium carbonate is listed, the cited patent also lists stearic acid and alginic acid (column 7, lines 18-29), so it is clear that the cited patent does not teach the use of only basic excipients, and does not guide one to make a composition having a pH of at least 8.

Applicants have carefully studied a variety of formulations containing the subject compounds, as is shown in the examples and disclosure of the specification, and have discovered that it is necessary to form the claimed composition having a pH of at least 8 in order to achieve the desired stability. The cited reference fails to teach this invention.

For the foregoing reasons, Applicants respectfully request the withdrawal of this rejection under § 102(e).

Claims 1-6, 10-11, 16 and 35-38 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over USPN 6,002,008 (Wissner, et al.) in view of Cotton, et al. (Int'l. J. of Pharmaceutics 1994, 109, 237-249). The Examiner has stated that Wissner, et al. teach a compound of formula I and the use of solid carriers and solid dosage forms, but has found that basic excipients are not taught by Wissner, et al. The Examiner has stated that Cotton, et al. teach basic excipients to stabilize L-649,923. The Examiner has concluded that it would have been obvious to combine basic excipients with a compound of the present invention to stabilize the composition and bring the pH to at least 8. Applicants traverse this rejection for the reasons set forth below.

Wissner, et al. fails to teach the claimed composition, as the Examiner has admitted. It teaches only the compound, not the stabilized formulation claimed by Applicants.

Applicants have discovered stabilized pharmaceutical compositions for the claimed cyano-quinoline amide compounds. L-649,923 is a gamma-lactone; it contains no cyano group, no quinoline ring system and no amide group. In short, it is a completely different class of compound than the compounds of the claimed composition. Therefore, Cotton, et al. teach nothing about how to make a stable composition of the presently claimed compounds. A formulation that may work for a gamma-lactone may well not work for a cyano-quinoline amide of the present invention. Additionally, the cited reference does not require a pH of at least 8, as claimed.

The Examiner has tried to combine these two references to show that it would have been obvious to make the claimed invention. However, the cited references are directed to completely different classes of compounds, and nothing in the cited references would suggest the combination that the Examiner has suggested. Absent some suggestion or motivation to combine, the invention cannot be said to be obvious based on a combination of these two references.

A skilled formulations chemist will understand that different types of chemical compounds may need very different excipients to form a stable and efficacious pharmaceutical composition, and that one cannot simply substitute a completely different type of active compound into a formulation with any reasonable certainty that the new formulation will be stable or will be pharmaceutically effective. Therefore, one skilled in the

art would not seek to combine the formulation ingredients according to Cotton, et al. with the compound of Wissner, et al.

Furthermore, neither reference teaches that the claimed composition must have a pH of at least 8. Therefore, even if these two references could be combined as the Examiner has suggested, they would still not teach the claimed invention. Additionally, if one sought to make the combination but did not select the "right" excipients from Cotton, et al., the present invention would not be obtained, and nothing in the cited art would lead one to make the right selection of excipient(s).

The Examiner has cited two unrelated references, selected an element of the invention from each using the Applicants' invention as a road map, and concluded that the invention must be obvious. The problem is that, absent prior knowledge of the invention, one would not consider these references together, and would certainly not know which elements to select and combine to assemble the claimed invention.

The cited references, whether taken individually or in combination, simply fail to teach or suggest the claimed invention as a whole.

For the foregoing reasons, Applicants respectfully request the withdrawal of this rejection of claims 1-6, 10-11, 16 and 35-38 under § 103(a).

The Examiner has rejected claims 35-38 under 35 U.S.C. § 103(a) as being unpatentable over USPN 6,002,008 (Wissner, et al.) in view of Cotton, et al. (Int'l. J. of Pharmaceutics 1994, 109, 237-249). This appears to duplicate part of the prior rejection. Applicants traverse this rejection, and believe that claims 35-38 are patentable for all the reasons set forth above with regard to the prior rejection. These product by process claims cover those formulations of claim 1 made by the recited process; as explained above, all formulations of claim 1 (including those of claims 35-38) are patentable over the cited art. The fact that certain process steps may be disclosed in the cited art does not render the novel claimed composition any less patentable. As the Examiner has noted, patentability of product-by-process claims depends on the patentability of the product itself. The cited references, whether taken individually or in combination, simply fail to teach or suggest the claimed invention as a whole.

For the foregoing reasons, Applicants respectfully request the withdrawal of this rejection of claims 35-38 under § 103(a).

The Examiner has also rejected claims 7-9 and 13-14 under 35 U.S.C. § 103(a) as being unpatentable over Wissner, et al. in view of Cotton, et al., and further in view of Makino, et al. (5,879,708). Applicants traverse for the following reasons.

Claims 7-9 and 13-14 are patentable over Wissner, et al and Cotton, et al. for the same reasons as those provided above with regard to the rejection of claim 1, et seq.

The Examiner has introduced Makino, et al. to show the enteric coating and the weight percentages of the excipients that are recited in the rejected claims. However, the Examiner once again is combining disparate references. This new reference is directed toward benzimidazoles. Thus, the Examiner suggests that a reference relating to benzimidazoles should be combined with a reference relating to gamma-lactones to teach how to make a formulation containing a cyano-quinoline amide compound. This is simply not logical. No knowledgeable formulation chemist would expect such a combination to be fruitful.

In most formulation inventions, the ingredients of the formulation can all be found in the art, but it is the unique combination of ingredients which constitutes the invention as a whole that is not in the prior art.

For these reasons, Applicant respectfully requests the withdrawal of the instant rejection of claims 7-9 and 13-14.

The Examiner has rejected claim 12 under 35 U.S.C. §103(a) as being unpatentable over Wissner, et al. in view of Cotton, et al., and further in view of Curatolo, et al. (US2003/0198674). Applicants traverse for the following reasons.

Claim 12 is patentable over Wissner, et al and Cotton, et al. for the same reasons as those provided above with regard to the rejection of claim 1, et seq.

The Examiner has cited Curatolo, et al. as teaching an immediate release form of a quinoline derivative. However, this reference does not provide the teachings or suggestions that the other cited references lack. For example, Curatolo, et al. do not teach a stabilized pharmaceutical composition of the claimed compound containing at least one basic excipient in a concentration sufficient to bring the pH of the composition to at least 8.

The three cited references, whether taken individually or in any combination, do not teach the claimed invention as a whole. Applicants respectfully request withdrawal of this rejection of claim 12.

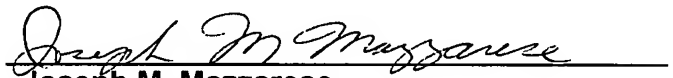
The Examiner has rejected claims 16-17 and 38 under 35 U.S.C. § 112, second paragraph, as having insufficient antecedent basis. Specifically, the Examiner says that they recite a compound having a N,N-dialkylaminoalkyl group of only 1 carbon atom rather than 3-12 carbons. Applicants traverse.

Applicants respectfully direct the Examiner's attention to the fact that the minimum number of carbon atoms that any N,N-dialkylaminoalkyl group can have is three, i.e., N,N-dimethylaminomethyl contains three methyl groups and, therefore, three carbon atoms. In the present case, N,N-dimethylamino-but-2-enoic acid contains 6 carbons, which does fall within the range of 3-12 carbons recited in claim 1. Therefore, the Examiner has erred in calculating the number of carbon atoms. For this reason, withdrawal of the rejection is requested.

The Examiner has rejected claim 17 under 35 U.S.C. § 112, second paragraph, as being indefinite in using "the compound comprises" in view of the election of species. Applicants disagree, but in view of the amendment to claim 17 the cited phrase is no longer in the claim. Therefore, this rejection is moot and withdrawal thereof is requested.

Applicants believe that claims 1-17 and 35-38 are patentable over the cited art and solicit allowance thereof at an early date.

No fee is believed to be due herewith, but should any fee be due it may be charged to Dep. Acct. #01-1425.



Joseph M. Mazzarese
Attorney for Applicants
Reg. No. **32,803**

Wyeth
Patent Law Department
Five Giralda Farms
Madison, NJ 07940
Tel. No. (973) 660-**7657**